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EVALUATION OF THE EFFECTIVENESS AND SAFETY OF OSTEOBIOS IN PREVENTIVE CARE AND TREATMENT OF OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN

INTRODUCTION

Osteobios is a complex low dose medicinal product consisting of potentiated mineral, animal and suis-organ components tropic to bone tissue and organs that regulate the metabolism of calcium in the body.

The medicinal product differs by its properties and mechanism of action from traditional antiosteoporotic medicinal products. Due to its complex structure (7 suis-organs, animal and mineral components, 5 of which are in - D10/D12, D30, D 200) Osteobios makes it possible to provide systemic therapy of disorders of calcium metabolism.

Its use facilitates balancing the activity of osteoclasts and osteoblasts, preventing the loss of calcium from bone tissue, stimulating the synthesis of protein components of the matrix, which leads to the improvement of bone structure.

– Today, methods of treatment with low dose medicinal products could expand treatment options. Over the past decades, this area CAM became widespread. However, clinical studies in accordance with the rules of evidence-based medicine for this group of medicinal products are essentially limited to specific applications of medicinal products with homeopathic composition. Nevertheless there are studies on Osteobios in the treatment of the diseases of gastrointestinal, respiratory and urinary tract, oral cavity, in the postoperative rehabilitation after orthopaedic surgery, gynaecologic abnormality involving disorders of calcium homeostasis in both adults and children.

DOSAGE AND METHOD OF ADMINISTRATION

Single dose for adults and children over 12 years is 10-12 drops. It should be administered 2-3 times daily, 30 minutes before meals or an hour after. Drops should be dissolved in 10-15 ml of water and drank, keeping for a few seconds in the mouth. Adults can drop the medicinal product directly under the tongue. Course of treatment is 1-2 months. Prophylactic courses can be held up to 3-4 times a year.

INDICATIONS FOR USE

I. Prevention of calcium metabolic imbalance and osteoporosis in patients with increased need for calcium:

- children in the period of intensive growth (4-6 and 10-15 years);
- women during pregnancy and lactation;
- professional athletes.

Prevention of primary osteoporosis and osteoporotic fractures:

- in perimenopausal and postmenopausal women;
- in the elderly and later period;
- with hereditary predisposition to osteoporosis (frequent fractures in a family history).

Prevention of secondary osteoporosis in:

- chronic diseases (endocrine, rheumatic, renal, gastrointestinal, arthritis, degenerative spine disease, etc.)
- long term use of corticosteroids, immunosuppressants, anticonvulsants, heparin, thyroxin, aluminium-containing antacids, etc.)
- ovarian hypoplasia after ovariectomy;
- prolonged immobilization.

II. Therapy of osteoporosis and disorders of calcium metabolism:

- senile, juvenile, idiopathic, postmenopausal osteoporosis;
- bone softening, including postpartum period and elderly;
- slow consolidation of fractures.

III. Support medicinal product in the treatment of hormone replacement therapy (HRT) and **antiresorbents**.

IV. Parodontosis, in complex the treatment of teeth diseases.
- ***Contraindications:*** none.
- ***Side effects:*** not found.
- ***Interaction with other medicines:*** within normal.

OBJECTIVE OF THE STUDY

To examine the efficacy and safety of **Osteobios** in the prevention and treatment of systemic osteoporosis in **postmenopausal women**.

TARGETS OF THE STUDY

1. To study the effect of Osteobios on the severity of vertebral pain in postmenopausal women with systemic osteoporosis.
2. To study the effect of Osteobios on bone mineral density in postmenopausal women with systemic osteoporosis.
3. To study safety of Osteobios when used in postmenopausal women with systemic osteoporosis.

STUDY DESIGN

Type of study
This clinical study was conducted as an open, controlled, parallel groups, randomized study.
Combined calcium and vitamin D medicinal product Calcemin advance, tablets, was used as a comparator product.

Description of the study
This study was conducted in accordance with the rules of the Good Clinical Practice.

– The study involved **30 postmenopausal women with systemic osteoporosis**.
Of these, 15 women were in the study group and the other enrolled women were in the comparison group. Patients of the study group (15 women) received Osteobios plus calcium and vitamin D (Calcemin advance).
Patients of the comparison group (15) received only calcium Calcemin advance.
All participants of the study were explained the conditions of the study, were suggested reading the "Information sheet for a patient", signed a written consent to participate in the study.
Before inclusion in the study each patient underwent clinical and instrumental examination in accordance with an established scheme.

After the determination of bone mineral density, patients who met the inclusion / exclusion criteria were enrolled in the study.

Patients of the study group received Osteobios and patients of the comparison group - the medicinal product Calcemin advance according to the schemes set up in the annotation.
The study lasted 6 months. Comprehensive examination, according to the study protocol, was conducted at the beginning of the treatment, and after 3 and 6 months according to the established protocol.
The data obtained from the study were evaluated by referring to the section scales and statistically processed.
Based on those results, conclusion on the efficacy and safety of the investigated medicinal product were done.

Randomization
Patients included in the study were distributed into groups - the study group and the comparison group – by means of a simple method of randomization.

STUDY MEDICINAL PRODUCTS

Study medicinal product
Name - Osteobios
Active ingredients: 100 ml of drops contain: Os suis D10 – 5.5 ml, Os suis D30 – 5.5 ml, Os suis D200 – 5.5 ml, Glandula parathyroidea suis D10 – 6 ml, Glandula parathyroidea suis D30 – 6 ml, Glandula parathyroidea suis D200 – 6 ml, Calcium carbonicum D12 – 6 ml, Calcium carbonicum D30 – 6 ml, Calcium carbonicum D200 – 6 ml, Calcium phosphoricum D12 – 6 ml, Calcium phosphoricum D30 – 6 ml, Calcium phosphoricum D200 – 6 ml, Calcium fluoratum D12 – 6 ml, Calcium fluoratum D30 – 6 ml, Calcium fluoratum D200 – 6 ml, Master aminoacid pattern (MAP) D3 – 5.5 ml, Calcitonin D6 – 6 ml.
Pharmaceutical form – solution
Manufacturer – Guna S.p.a., Milan, Italy.

Comparative product (Comparator)
Name - Calcemin advance
Active ingredients: 1 tablet contains: calcium citrate -217 mg, calcium carbonate - 1312 mg, vitamin D3 (cholecalciferol) - 200 IU, magnesium - 40 mg, zinc – 7.5 mg, copper - 1 mg, manganese – 1.8 mg, borium - 250 µg.
Pharmaceutical form – tablets
Manufacturer – Bayer HealthCare.

CONTINGENT AND METHODS OF THE STUDY

Number of the study subjects
The study included 30 postmenopausal women, divided into II groups depending on the bone mineral density (BMD) and prescribed therapy:
- **I group** – study group - **15** postmenopausal women with systemic osteoporosis who received Osteobios (20 drops, 3 times

a day, 30 minutes before meals or one hour after meals daily) and Calcemin advance (1 tablet, 2 times a day, with meals daily).

• **II group** - comparison group - **15** postmenopausal women with systemic osteoporosis who received Calcemin advance (1 tablet, 2 times a day, with meals daily).

Inclusion criteria

- Postmenopausal women.
- Presence of vertebral pain more than VAS 4 points.
- A group of systemic osteoporosis in terms of BMD ″ (-2.5) SD at the lumbar spine and / or femur without osteoporotic fracture or BMD ″ (-2.0) SD with the presence of osteoporotic fractures (vertebral bodies, femoral neck bone, distal forearm);
- No administration of osteotropic medicinal products for 1 month prior to the study, except preparations of calcium and vitamin D.

GROUP	I (n=15)	II (n=15)
Age, years	65.4±6.75	62.8±6.45
Weight, kg	64.4±9.39	65.4±10.54
Height, cm	159.3±4.48	161.1±7.75
Age of menopause, years	45.0±9.19	47.3±4.31

TAB. 1
General characteristics of the II groups.

The general characteristics of the examined women according to the study group are presented in TABLE 1.

Exclusion criteria

- The disease presence of severe chronic diseases (liver, kidney, endocrine and infectious disease, connective tissue diseases).
- Presence of risk factors that could affect the structural and functional state of bone (administration of corticosteroids, anticonvulsants for three years, radiation effects).
- Availability of high-energy fractures and trauma in the medical history.
- Secondary osteoporosis of any origin.
- Malignant neoplasm.

The study excluded patients with at least one of the above-mentioned exclusion criteria.

Discontinuation criteria

- Individual intolerance to the study medicinal products.
- The occurrence of severe and / or undesirable side effects in the patient during the study.
- Significant deterioration of the general condition during the study, requiring the appointment of not recommended medicines.
- Failure to keep to the regime of administration of the medicinal products.
- Patient refusal to continue participation in the study (drop out).

Scheme of examination of the patients

To evaluate the efficacy and tolerability of the study medicinal products, the examination of the patients was conducted using clinical, instrumental and laboratory methods.

Medical history data

- Past medical history.
- Determination of risk factors for disorder of bone tissue.
- Medical history on osteoporosis or osteopenic syndrome with the determination of their beginning, the course, prior treatment, availability of low-energy fractures.
- Concomitant diseases and their treatment.

Methods of the study

1. General clinical examination.
2. Neuro-orthopedic examination.
3. Radiography of lumbar and thoracic spine for diagnosis establishment.
4. Evaluation of the severity of vertebral pain by McGill questionnaires and 11-component Visual Analogue Scale (VAS).
5. Evaluation of quality of life by EuroQull-5D questionnaire.
6. Evaluation of daily and life activities by ECOS-16 and Roland-Morris questionnaires.
7. Determination of bone mineral density by dual-energy X-ray absorptiometry.
8. Determination of markers of bone mineral metabolism for women of the study group and comparison group with systemic osteoporosis.

Follow-up was conducted for **6 months** - before treatment, after **3** and **6 months**.

The dynamics of parameters was determined by the formulae: Δ of the value (%) = [(value after – value before) / value before] x 100.

Statistical analysis was performed using the software package "Statistika 6.0", using Student's test for related samples and unifactor analysis of variance Anova.

The difference of values was considered significant at $p < 0.05$.

TREATMENT

Schemes of prescription of study the medicinal product and comparator

Osteobios was administered daily: 20 drops, 3 times a day, 30 minutes before meals or one hour after meal.

It was recommended to dissolve the drops in 10-15 ml of water before use and drink, holding for a few seconds in the mouth.

Comparator - Calcemin advance was recommended to administer daily: 1 tablet 2 times a day with meals.

– The course of treatment for each patient was **6 months**.

Concomitant treatment

Clinical study of Osteobios was conducted without basic treat-

ment of the underlying disease.
It was allowed to use medicinal products to correct co-morbidity, but those who do not affect the *status* of bone mineral density and its functioning (e.g., medicinal products for blood pressure correction).
During the study, the patients were not treated by any other osteotropic medicinal product and/or medicinal products affecting bone metabolism.

EVALUATION OF THE EFFECTIVENESS

According to the study of the characteristics of vertebral pain in postmenopausal women with systemic osteoporosis during treatment with Osteobios and Calcemin advance it was set significant decrease of McGill Questionnaire values after 6 months of treatment, describing the pain in the thoracic spine in the study group [descriptors index (t = 13.0, p = 0.01), ranks index (t = 11.0, p = 0.02), pain index (t = 17.0, p = 0.05)]. In the comparison group significant reduction in the severity of pain in the thoracic spine was also found after 6 months of therapy for index descriptors (t = 5.0, p = 0.02) and pain index (t = 6.5, p = 0.04) (TABLE 2).
Time course of indexes after 6 months in the study group and the comparison group was the following: for the descriptors index 52% and 37%, ranks index 54% and 27%, pain index 47% and 24%, respectively.

GROUP	Before treatment	After 3 months	After 6 months
	Descriptors index		
I	5.93±5.22	5.33±4.23	3.87±4.17*
II	6.00±4.19	5.75±4.45	4.58±4.85*
F, p	F=0.58; p=0.45	F=0.13; p=0.73	F=0.01; p=0.94
	Ranks index		
I	9.53±9.88	9.00±8.76	5.67±5.96*
II	9.92±7.60	10.75±8.86	7.92±8.39
F, p	F=0.33; p=0.57	F=0.05; p=0.83	F=0.16; p=0.69
	Pain index		
I	3.83±2.19	3.07±2.12	2.33±2.13*
II	3.60±1.68	3.25±1.91	2.75±1.96*
F, p	F=1.52; p=0.23	F=0.78; p=0.39	F=0.07; p=0.79

** Probable difference compared with baseline value, p<0.05.*

TAB. 2
McGill Questionnaire indexes for the thoracic spine.

The results of the analysis of the variance revealed no differences in indexes of the McGill Questionnaire for the thoracic spine in the two groups during the course of the treatment.
Severity of pain in the lumbar spine according to the index of pain decreased significantly during the treatment in patients of the study group after 3 (t = 7.5, p <0.01) and 6 (t = 6.6, p <0.01) months, and in the comparison group - only after 3 months (t = 4.5, p = 0.03).
There were no probable differences of descriptors and ranks indexes during the course of treatment in both groups (TABLE 3).

The time course of MacGill Questionnaire for the lumbar spine after 6 months was in the study group and comparison group as follows: descriptors index - 26% and 15%, ranks index - 20% and 4%, pain index - 35% and 28%, respectively. The results of analysis of variance revealed no differences in indexes of the McGill Questionnaire for the lumbar spine between the groups during the course of treatment.
According to the study of the characteristics of vertebral pain according to the 11-component Visual Analogue Scale it was established probable reduction of pain in the thoracic spine in patients of the study group by VAS-1 (pain at the time of examination) at 6 months (t = 6.5, p = 0.03), VAS-2 (typical or medium

GROUP	Before treatment	After 3 months	After 6 months
	Descriptors index		
I	6.53±4.27	6.20±4.13	5.27±4.43
II	8.50±5.11	7.67±4.92	7.58±5.88
F, p	F=1.08; p=0.31	F=0.22; p=0.64	F=2.12; p=0.16
	Ranks index		
I	10.47±8.78	11.27±8.29	9.4±8.8
II	17.92±13.77	15.50±10.96	15.17±13.46
F, p	F=2.68; p=0.11	F=1.64; p=0.21	F=5.53; p=0.03
	Pain index		
I	4.13±1.77	3.47±1.77*	2.80±1.82*
II	5.25±1.96	4.03±1.87*	4.00±2.13
F, p	F=0.21; p=0.65	F=0.36; p=0.56	F=0.54; p=0.47

** Probable difference compared with baseline value, p<0.05.*

TAB. 3
McGill Questionnaire indexes for the lumbar spine.

Before treatment				
VAS	**Group I**	**Group II**	**F**	**p**
VAS-1. Pain at time of examination	2.40±2.03	2.91±1.93	1.19	0.28
VAS-2. Most typical or medium pain level	2.87±2.26	2.92±1.51	1.98	0.17
VAS-3. Pain level at time of the best periods of the disease	1.87±1.36	1.83±1.69	0.63	0.44
VAS-4. Pain level at time of the worst periods of the disease	4.13±3.14	5.00±3.10	0.07	0.79
VAS-5. Starting pain	2.13±2.26	2.75±2.38	0.17	0.68
VAS-6. Pain at continuous walking	3.20±2.48	3.25±2.26	0.80	0.38
VAS-7. Pain at continuous rest (at night)	1.73±1.75	2.00±2.17	0.001	0.97
VAS-8. Permanent (steady) pain	1.87±1.51	2.20±2.47	1.08	0.31
VAS-9. Pain at walking upstairs	1.53±1.36	2.75±2.05	1.63	0.21
VAS-10. Pain at walking downstairs	1.47±1.19	2.58±2.19	1.33	0.26
VAS-11. Pain at walking on level ground	1.67±1.39	2.00±1.95	0.19	0.67
After 3 months of treatment				
VAS	**Group I**	**Group II**	**F**	**P**
VAS-1. Pain at time of examination	2.20±1.97	3.67±2.34	0.41	0.53
VAS-2. Most typical or medium pain level	2.33±2.19	3.00±2.41	0.59	0.45
VAS-3. Pain level at time of the best periods of the disease	1.27±1.09*	2.42±1.78	2.11	0.06
VAS-4. Pain level at time of the worst periods of the disease	4.00±3.23	3.92±3.18	0.005	0.95
VAS-5. Starting pain	1.60±1.45	2.17±2.41	1.17	0.29
VAS-6. Pain at continuous walking	2.40±2.09	3.67±2.84	0.77	0.39
VAS-7. Pain at continuous rest (at night)	1.20±1.61	2.00±2.17	0.19	0.66
VAS-8. Permanent (steady) pain	1.53±1.51	2.00±2.26	0.98	0.33
VAS-9. Pain at walking upstairs	1.87±2.07	3.00±2.26	0.02	0.88
VAS-10. Pain at walking downstairs	1.53±1.59	2.58±2.23	0.46	0.51
VAS-11. Pain at walking on level ground	1.27±1.44	2.50±2.35	1.78	0.19
After 6 months of treatment				
VAS	**Group I**	**Group II**	**F**	**P**
VAS-1. Pain at time of examination	1.13±2.07*	2.83±2.04	0.00	0.99
VAS-2. Most typical or medium pain level	1.40±1.88*	3.08±2.07	0.02	0.89
VAS-3. Pain level at time of the best periods of the disease	0.93±1.49*	1.83±1.27	0.08	0.78
VAS-4. Pain level at time of the worst periods of the disease	2.80±3.21*	4.08±3.29	0.04	0.84
VAS-5. Starting pain	0.87±1.51*	2.42±2.07	1.59	0.22
VAS-6. Pain at continuous walking	1.53±2.53*	2.92±1.83	1.13	0.29
VAS-7. Pain at continuous rest (at night)	1.13±1.81	1.75±1.06	2.58	0.12
VAS-8. Permanent (steady) pain	0.87±1.56*	2.00±1.81	0.87	0.36
VAS-9. Pain at walking upstairs	0.73±1.28	2.50±1.73	1.04	0.32
VAS-10. Pain at walking downstairs	0.80±1.37	2.50±1.88	1.47	0.24
VAS-11. Pain at walking on level ground	0.80±1.57*	1.75±1.29	0.002	0.96

TAB. 4

VAS indexes of the thoracic spine.

** Probable difference compared with baseline value, p<0.05.*

Before treatment				
VAS	**Group I**	**Group II**	**F**	**P**
VAS-1. Pain at time of examination	3.27±2.52	4.50±2.19	0.55	0.47
VAS-2. Most typical or medium pain level	3.87±2.09	4.17±1.59	2.06	0.16
VAS-3. Pain level at time of the best periods of the disease	2.20±1.37	2.83±2.08	2.27	0.14
VAS-4. Pain level at time of the worst periods of the disease	5.60±3.27	6.91±2.27	2.82	0.11
VAS-5. Starting pain	3.4±2.56	3.83±2.44	0.04	0.83
VAS-6. Pain at continuous walking	4.13±2.67	4.17±2.59	0.15	0.70
VAS-7. Pain at continuous rest (at night)	2.67±1.88	3.33±2.15	0.00	0.98
VAS-8. Permanent (steady) pain	2.67±1.79	3.50±2.02	0.09	0.76
VAS-9. Pain at walking upstairs	3.00±2.20	3.83±1.69	0.89	0.35
VAS-10. Pain at walking downstairs	2.87±2.64	3.75±1.82	0.59	0.45
VAS-11. Pain at walking on level ground	2.80±2.48	3.00±1.21	5.08	0.03
After 3 months of treatment				
VAS	**Group I**	**Group II**	**F**	**P**
VAS-1. Pain at time of examination	2.20±1.47*	3.42±2.35	2.43	0.13
VAS-2. Most typical or medium pain level	3.13±1.73	4.08±2.47	1.10	0.30
VAS-3. Pain level at time of the best periods of the disease	1.67±0.82	2.67±1.61	5.30	0.03
Before treatment				
VAS	**Group I**	**Group II**	**F**	**P**
VAS-4. Pain level at time of the worst periods of the disease	5.33±2.87*	6.17±2.33	1.19	0.29
VAS-5. Starting pain	2.20±1.61*	2.42±2.68	1.20	0.28
VAS-6. Pain at continuous walking	2.80±2.48*	4.75±2.34	0.04	0.84
VAS-7. Pain at continuous rest (at night)	2.27±1.83	2.75±2.34	0.45	0.51
VAS-8. Permanent (steady) pain	1.80±1.57*	2.75±2.26	1.08	0.31
VAS-9. Pain at walking upstairs	3.13±2.17	2.92±2.23	0.01	0.93
VAS-10. Pain at walking downstairs	2.67±2.09	2.92±2.15	0.02	0.88
VAS-11. Pain at walking on level ground	2.47±2.33	3.08±1.92	1.41	0.25
After 6 months of treatment				
VAS	**Group I**	**Group II**	**F**	**P**
VAS-1. Pain at time of examination	1.80±1.97*	3.33±2.61	0.72	0.40
VAS-2. Most typical or medium pain level	3.27±2.22	3.42±2.61	0.01	0.91
VAS-3. Pain level at time of the best periods of the disease	1.67±1.79	2.00±1.54	0.66	0.42
VAS-4. Pain level at time of the worst periods of the disease	5.33±2.92	4.83±2.82*	0.14	0.71
VAS-5. Starting pain	2.33±1.99	2.50±2.35*	0.29	0.59
VAS-6. Pain at continuous walking	3.27±2.76	3.58±2.11	2.34	0.14
VAS-7. Pain at continuous rest (at night)	2.00±1.65	1.83±0.94	0.06	0.81
VAS-8. Permanent (steady) pain	1.80±1.14	2.42±2.57	4.22	0.05
VAS-9. Pain at walking upstairs	2.40±2.23	2.83±2.17	0.49	0.49
VAS-10. Pain at walking downstairs	2.53±2.61	2.75±2.34	0.12	0.73
VAS-11. Pain at walking on level ground	1.87±2.13*	2.25±1.86	1.43	0.24

TAB. 5

VAS indexes of the lumbar spine.

** Probable difference compared with baseline value, p<0.05.*

pain level) (t = 3.5, p = 0.01), VAS-4 (pain level at time of the worst periods of the disease) (t = 2.5, p = 0.03), VAS-5 (starting pain at the beginning of the movement) (t = 1.5, p = 0.05), VAS-6 (pain at continuous walking) (t = 9.0, p = 0.03), VAS-8 (permanent steady pain) (t = 8.0, p = 0.03), VAS-11 (pain at walking on level ground) (t = 6.5, p = 0.03) and for VAS-3 (pain level at time of the best periods of the disease) after 3 (t = 2.5, p = 0.02) and 6 (t = 5.0, p = 0.01) months.
In the comparison group probable differences in terms of 11-component VAS were not found during the study. However, by the results of the analysis of variance no probable differences were revealed between groups (TABLE 4).

According to the analysis of the severity of pain in the lumbar spine according to VAS in patients of the study group it was found a **significant reduction** of pain by VAS-1 (pain at the time of examination) after 3 (t = 8.5, p <0.01) and 6 months (t = 6.5, p <0.01), 3 months by VAS-4 (pain level at time of the worst periods of the disease) (t = 4.5, p = 0.02), VAS-5 (starting pain at the beginning of the movement) (t = 5.0, p = 0.02), VAS-6 (pain at continuous walking) (t = 4.0, p = 0.05), VAS-8 (permanent steady pain) (t = 3.5, p = 0.02) and after 6 months of therapy by VAS-11 (pain at walking on level ground) (t = 6.0, p = 0.02).

In the comparison group significant reduction of pain in the lumbar spine was found after 6 months by VAS-4 (pain level at time of the worst periods of the disease) (t = 2.5, p <0.01) and VAS-5 (starting pain at the beginning of the movement) (t = 7.0, p = 0.02) (TABLE 5).

The results of variance analysis showed significantly greater reduction of pain in the lumbar spine after 3 months by VAS-3 (pain level at time of the worst periods of the disease) (F = 3.5, p = 0.03) and 6 months by VAS-8 (permanent steady pain) (F = 4.2, p = 0.05).

Analysis of peculiarities of the changes in the bone mineral density during the treatment with Osteobios and Calcemin advance found no significant increase of BMD at the trochanter of femoral bone, femoral bone, femoral neck, lumbar spine, skeleton, middle third of the radial bone, radial bone, and ultradistal part of the radial bones in both groups, both during the period of treatment, and between the groups. It should be noted, that no significant decrease of BMD was detected in both groups during the treatment (TABLE 6).

GROUP	Before treatment	After 3 months	After 6 months
BMD of the trochanter of femoral bone, g/cm²			
I	0.652±0.12	0.656±0.11	0.668±0.11
II	0.693±0.11	0.691±0.13	0.678±0.12
F, p	F=0.002, p=0.96	F=0.66, p=0.43	F=0.07, p=0.80
BMD of the femoral bone, g/cm²			
I	0.806±0.12	0.803±0.12	0.815±0.12
II	0.838±0.12	0.833±0.13	0.824±0.12
F, p	F=0.17, p=0.68	F=0.27, p=0.60	F=0.01, p=0.91
BMD of the femoral neck, g/cm²			
I	0.741±0.11	0.745±0.11	0.751±0.12
II	0.779±0.08	0.777±0.08	0.766±0.09
F, p	F=1.07, p=0.31	F=1.30, p=0.26	F=0.74, p=0.40
BMD of the lumbar spine, cm²			
I	0.871±0.08	0.873±0.08	0.888±0.07
II	0.858±0.08	0.848±0.08	0.851±0.07
F, p	F=0.07. p=0.79	F=0.28, p=0.60	F=0.004, p=0.95
BMD of the skeleton, g/cm²			
I	0.971±0.08	0.974±0.08	0.969±0.09
II	0.953±0.08	0.966±0.07	0.963±0.07
F, p	F=0.02, p=0.88	F=0.03, p=0.88	F=0.24, p=0.63
BMD of the middle third of the radial bone, g/cm²			
I	0.563±0.097	0.546±0.097	0.558±0.099
II	0.515±0.07	0.512±0.08	0.517±0.08
F, p	F=2.33, p=0.14	F=0.78, p=0.39	F=1.07, p=0.31
BMD of the radial bone, g/cm²			
I	0.448±0.08	0.432±0.08	0.439±0.08
II	0.411±0.06	0.412±0.06	0.410±0.06
F, p	F=3.14, p=0.09	F=2.55, p=0.12	F=1.31, p=0.26
BMD of the ultradistal part of the radial bone, g/cm²			
I	0.294±0.06	0.279±0.06	0.288±0.06
II	0.271±0.05	0.277±0.05	0.271±0.05
F, p	F=0.30, p=0.59	F=0.495, p=0.49	F=0.37, p=0.55

TAB. 6
Bone mineral density.

GROUP	Before treatment	After 3 months	After 6 months
	Propeptides of type I procollagen, ng/ml		
I	45.28±29.26	41.66±17.03	35.18±19.20
II	43.26±29.73	42.46±21.77	41.93±20.86
F, p	F=0.09, p=0.76	F=0.34, p=0.57	F=0.43, p=0.52
	Vitamin D, nmol/L		
I	27.30±18.78	32.71±19.05	32.31±19.30
II	41.69±14.28	47.98±13.33	45.68±20.19
F, p	F=1.34, p=0.26	F=0.63, p=0.44	F=0.004, p=0.95
	Osteocalcin, ng/ml		
I	28.61±17.66	27.11±8.19	25.09±8.38
II	25.65±11.43	25.49±8.93	25.86±9.78
F, p	F=0.83, p=0.37	F=0.34, p=0.57	F=0.92, p=0.35
	β-terminal telopeptides of type I collagen, ng/ml		
I	0.43±0.17	0.37±0.12	0.37±0.18
II	0.53±0.33	0.46±0.27	0.44±0.25
F, p	F=6.04, p=0.21	F=5.87, p=0.20	F=1.59, p=0.22
	Parathormone, ng/ml		
I	50.67±22.91	53.07±14.49	49.05±18.57
II	42.00±10.44	44.95±19.87	55.07±13.33
F, p	F=4.27, p=0.06	F=2.09, p=0.16	F=0.19, p=0.67

TAB. 7
Values of bone metabolism markers during the treatment.

GROUP	Before treatment	After 3 months	After 6 months
	Roland-Morris		
I	4.73±4.37	4.00±3.72	3.47±3.78
II	4.75±4.11	4.58±3.34	4.58±3.70
F, p	F=0.17, p=0.68	F=0.22, p=0.64	F=0.09, p=0.76
	EuroQol 1		
I	3.20±1.61	2.93±1.75	2.53±2.03
II	41.69±14.28	47.98±13.33	45.68±20.19
F, p	3.58±1.78	3.42±1.62	3.33±1.87
	EuroQol 2		
I	0.87±0.74	0.67±0.82	0.47±0.64
II	0.67±0.89	0.83±0.71	0.75±0.62
F, p	F=1.61, p=0.22	F=1.09, p=0.31	F=0.26, p=0.61
	ECOS–16		
I	37.07±13.39	38.07±12.49	35.6±13.73
II	40.92±11.55	42.67±8.64	41.67±9.63
F, p	F=0.52, p=0.48	F=0.93, p=0.34	F=0.15, p=0.69

TAB. 8
Indexes of life quality and daily activity during the treatment.

- Time course of BMD during treatment for the patients of the study group was after 3 and 6 months, respectively ΔBMD of the **lumbar spine** 0.2% and 1.6%; ΔBMD of the **skeleton** 0.4% and 0.7%; ΔBMD of the **radial bone** 0.5% and 0.6%; ΔBMD of the **femoral neck** 0.6% and 0.8%.

- In the comparison group, the corresponding figures were ΔBMD of the **lumbar spine** -1.1% and -0.7%; ΔBMD of the **skeleton** 0.5% and 0.9%; ΔBMD of the **radial bone** 0.4% and 0.1%; ΔBMD of the **femoral neck** -0.2% and -1.8%.

The results of the analysis of variance revealed no significant difference in the time course of BMD indexes between the groups.

The analysis of bone metabolism also showed no significant changes in biochemical markers throughout the study period in patients both of the study and the comparison group (TABLE 7).

No significant differences were found between the groups in terms of biochemical markers of bone metabolism.

According to Roland-Morris and ECOS-16 Questionnaires no significant changes of these indexes were detected during the study in both groups and between groups, as evidenced by the results obtained by the analysis of Euro-Qol and EuroQol 2 Questionnaires (TABLE 8).

EVALUATION OF SAFETY OF OSTEOBIOS

During the study the following adverse events were recorded: one patient within

two weeks of the beginning of the therapy with Osteobios experienced palpitation, drowsiness, increased blood pressure of moderate severity, and required additional treatment.

The product was withdrawn, and patient's condition returned to normal. The second patient during the first three months was additionally diagnosed with moderate severity ulcerative colitis, not related to the study medicinal product, but required additional treatment and discontinuation of the study medicinal product.
– No adverse events were recorded in patients of the comparison group during the study period.

CONCLUSIONS

The administration of the low dose medicinal product Osteobios for 6 months in postmenopausal women promotes the reduction of the severity of vertebral pain, stabilizing the processes of bone tissue loss and its metabolism. Osteobios can be used in a complex therapeutical system for the prevention of osteoporosis in postmenopausal women.

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